

### REMARKS

This is in response to the Office Action mailed March 12, 2002.

Claims 1 and 16 have been amended to specify that the concentration of the water structure-making substance in the solution is at least about one molar. Support for that limitation is throughout the specification, particularly the Examples. See, e.g., Tables 1-1 to 1-6; 1-11 to 1-12; 1-17 to 1-23; and 2-1 to 2-6. In addition, claims 31-32 are amended to recite the effect of partial duplex unwinding. Support for that is at, e.g., page 10, lines 6-33.

### Specification

Per the Examiner's request, the present amendment requests entry of an Abstract of the disclosure.

### Claim Objection

Reconsideration and withdrawal of the objection to claims 31 and 32 are respectfully requested. By virtue of the present amendment, those claims have been amended in accordance with the Examiner's helpful suggestion to ensure antecedent agreement with the claims from which they depend. No change in claim scope is intended or believed made.

35 U.S.C. §112, first paragraph

Reconsideration and withdrawal of the rejection of claims 1-32 under 35 U.S.C. §112, first paragraph, for alleged lack of enablement are respectfully requested. The Action alleges that the specification does not provide enablement for enhancing stability of triplexes within a living cell. Applicants respectfully traverse. The present specification does indeed provide guidance for use of the present methods within a cell.

For example, the Examiner's attention is respectfully directed to page 5, lines 3-11 of the present specification. There, it is taught that due to toxicity concerns, one must be mindful of the nature and concentration of the substances that can be used. It is further disclosed that cationic lipids are preferred when working with cells. It is respectfully submitted that that is an adequate teaching of how to use the present invention *in vivo*. The Action admits that the skill of those in the present art is high (page 4, item F), and therefore the foregoing is an adequate teaching to enable one to use the present inventions in cells.

Reconsideration and withdrawal of the rejection of claims 1-15, 31 and 32 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification are respectfully requested. The Action essentially alleges that the limitation that the water structure-making substance is added in

greater than a stoichiometric amount is new matter and lacks adequate written description in the specification as filed. While Applicants disagree with the Examiner's contention, by virtue of the present amendments to claims 1, 31 and 32, the objectionable language has been removed. The rejection is now moot.

**35 U.S.C. §112, second paragraph**

Reconsideration and withdrawal of the rejection of claim 32 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite are respectfully requested. The Action alleges that there is insufficient antecedent basis for greater than a stoichiometric amount limitation in claim 32. The term has been removed from claim 32, thus rendering the rejection moot.

**35 U.S.C. §102**

Reconsideration and withdrawal of the rejection of claims 1-2, 4-5, 9, 14, 16-17, 19-20, 24, 29, and 31-32 under 35 U.S.C. §102(b) as being anticipated by Kiyama are respectfully requested.

As acknowledged in the Action, Kiyama adds CTAB at a concentration of 100  $\mu$ M, whereas the present claims require that the water structure-making substance be present at a

concentration of at least about one molar. Thus, Kiyama cannot anticipate any of the present claims.

Reconsideration and withdrawal of the rejection of claims 1, 7-8, 14-16, 22-23 and 29-32 under 35 U.S.C. §102(b) as being anticipated by Shimizu are respectfully requested. Shimizu is relied on as showing the addition of 100 mM sodium acetate (to buffer at pH 5), 1M NaCl and 1mM oligonucleotide in the experiment summarized in Table 1. As shown in paragraph 12 of the Fresco Declaration filed September 28, 2000, Shimizu discloses enhancement of third strand binding stability by using base analogs as part of the third strand. There is no disclosure of enhancement due to water structure-making ability of the added salt; nor is that salt added at a water structure-making concentration. Moreover, it is respectfully submitted that the sodium acetate used by Shimizu is not within the scope of the present claims. All claims exclude the use of alkali metal cations by themselves as water structure-making substances. (See claim 1 clause a and claim 16 clause a). Thus, Shimizu cannot anticipate any of the present claims.

Reconsideration and withdrawal of the rejection of claims 1, 11-16, and 26-32 under 35 U.S.C. §102(b) as being anticipated by Moser are respectfully requested. Moser reports that upon addition of 40% ethylene glycol, the EDTA-Fe(II) cleaves the duplex with approximately ten-fold greater catalytic efficiency.

Nowhere is it made clear where the site of action is, whether it affects the behavior of the catalytic agent or the nature or stability of the triplex. Moreover, Moser reports that the addition of ethylene glycol at 20% by volume in some cases does not increase cleavage efficiency, thus suggesting some mechanism other than that described in the present application.

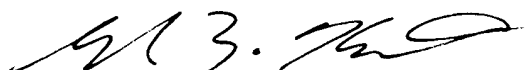
Reconsideration and withdrawal of the rejection of claims 1, 6, 14, 16, 21, 29 and 31-32 under 35 U.S.C. §102(b) as anticipated by Spink are respectfully requested. Spink is directed to triplex stabilization resulting from the addition of up to 20% (w/v) of PEG. That amount of PEG, however, is less than the amount recited in the present claims<sup>1</sup>, hence Spink cannot anticipate.

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<sup>1</sup>20% w/v means that there are 200 grams of PEG per liter of solution. Because Spink used PEGs having molecular weights of 400, 1000, 3400 and 8000, it follows that the molar concentration for each material was 0.5 M, 0.2 M, .06 M and .025 M, respectively.

It is respectfully submitted that the case is in condition  
for allowance.

Respectfully submitted,



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